REMARKS

In response to the Office Action mailed on December 10, 2003, Applicants have cancelled claims 1-40 and 46-62, added claims 63-65, and amended claims 41-45. Claims 41-45 and 63-66 remain pending after entry of the amendments.

The Office Action objected to the specification because it refers to trademarked products (DNAZOL™, TWEEN-20™ and DELTAPAC™). Applicants have revised these terms in the specification by capitalizing them, inserting a "TM" symbol and, where appropriate, including the generic terminology for the product.

The Office Action objected to the term "autobody" in claim 45. This typographical error has been corrected, and the word now reads "autoantibody."

The Office Action also rejected the claims under 35 U.S.C. § 112 because "central nervous systems disorders" are allegedly not sufficiently enabled by the specification. In a spirit of cooperation, Applicants have amended the claims to cover the diagnosis of "neurologic ischemic deficits." Applicants reserve the right to claim other central nervous system disorders by way of divisional or continuing application.

The Office Action also maintains that the claimed invention is either anticipated or obvious based upon certain prior art references. At the outset, Applicants note that the Office Action does not cite any prior art in which an ischemic event was diagnosed by detecting a panel of biomarkers that included NR2 peptides and NR2 agonists or antagonists. The Office Action cites Dambinova (1997) (the inventor for this application), and points out that Dr. Dambinova tested for NR2A autoantibodies, glutamate and aspartate in this publication.

The publication does not anticipate the claimed invention because the pending claims require the diagnosis to be via latex agglutination, and Dambinova (1987) discloses testing via undisclosed alternative methods (presumably ELISA and HPLC). As discussed below, the use of latex agglutination over the methods of the prior art surprisingly and unexpectedly increases the reliability of the diagnosis.

Dambinova (1997) also does not anticipate the pending claims because the pending claims require that a "diagnosis" occur. This term implies that the method is being performed at a time when it can have some therapeutic benefit, such as when it is actually being used to detect or predict a stroke or TIA, or to monitor the progress of therapy after a stroke has occurred. The

term also implies that the results of the test will be matched to the patient for whom the test is performed. To emphasize this critical point, claim 66 has been added reciting the fact that the results of the diagnosis are reported to the patient. Dr. Dambinova was not concerned with such real-time diagnoses of ischemic events when she published Dambinova (1997), but was instead looking for biomarkers in blood samples well after the ischemic event. The tests that she performed were not used to diagnose the health of the patients from whom the blood samples were taken.

The Office Action also maintains that it would have been obvious to combine an NR2 test with a test for glutamante, aspartate or homocysteine test based upon the teachings of Dambinova (1997), Daggert and Lipton (1997). However, the only reference that discloses testing of NR2 peptides in combination with an NR2 agonist or antagonist is Dambinova (1997), and it specifically reports in column 2 of page 153 that "A comparison of glutamate and aspartate concentration in CSF of patients did not correlate with severity of brain ischemic stroke and NR2A autoantibodies level." If anything, therefore, the prior art taught away from combining a panel of assays by indicating that one assay would not improve the diagnostic accuracy or reliability of the other.

In addition, Applicants have presented significant unexpected results from using latex agglutination instead of the HPLC reported in the prior art. As stated in Example 6 of the specification,

> With respect to predictive efficiency, however, LA showed a surprising improvement over HPLC. For example, the LA method improved the positive predictive efficiency of patients with TIA and acute stroke on the basis of glutamate content to more than 63 % (Tables 1, 3). The negative predictive value for healthy patients was similarly improved when using the LA technique (Tables 3, 4).

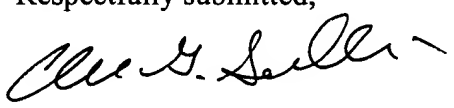
Tables 1 and 3 illustrate improved predictive value using latex agglutination for TIA patients (55.6 v. 66.4% predictive value), pre-stroke patients (44.4 v. 55.6% predictive value) and acute stroke patients (58.1 v. 64.5% predictive value). Tables 1 and 3 demonstrate that the latex agglutination method of the present invention is surprisingly superior over the HPLC methods of the prior art, and further prove the patentability of the claimed invention.

CONCLUSION

Applicant trusts that this communication is fully responsive to the pending Office Action. Should the Examiner have any further questions concerning this matter, the Examiner is invited to contact the undersigned at 404-572-3513.

A petition for a one-month extension extending the time within which to respond to April 10, 2004oncurrently herewith. Please grant any additional extension of time required to enter this response and charge any additional fees, or credit any overpayment to Deposit Account No. 11-0980.

Respectfully submitted,



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